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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/644,410	08/20/2003	Jay M. Short	1460-32	7934

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DIVERSA CORPORATION
4955 DIRECTORS PLACE
SAN DIEGO, CA 92121

EXAMINER	
STEELE, AMBER D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 03/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/644,410	SHORT, JAY M.	
	Examiner	Art Unit	
	Amber D. Steele	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-40* is/are pending in the application.

4a) Of the above claim(s) *5-10,12-22,24,27-33,37,38 and 40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-4, 11, 23, 25-26, 34-36, and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10-14-05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 2-40 are currently pending.

Claims 2-4, 11, 23, 25-26, 34-36, and 39 are currently pending and under consideration.

Claim 1 was canceled by Applicant in the Amendment received on August 20, 2003.

Election/Restrictions

2. Applicant's election of Group I (claims 2-5, 10-11, 12-26, and 34-40) in the reply filed on December 5, 2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Claims 6-9, 12-22, and 27-33 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on December 5, 2005.

4. Applicant's election of homologous first and second nucleic acids as the species of first and second nucleic acid homology, coupling mono- and oligonucleotides as the species of providing step; hybridization in vitro as the species of hybridization step, using polymerase as the species of polymerase, at least 3 oligonucleotide member types as the species of number of oligonucleotide member types, and homologous members in equimolar amounts as the species of amount of oligonucleotide member types in the reply filed on December 5, 2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed

errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

5. Claims 5, 10, 24, 37-38, and 40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on December 5, 2005.

Priority

6. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. [1] as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 09/185,373 (U.S. Patent 6,335,179), fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. U.S. Patent 6,335,179 fails to disclose codon-varied oligonucleotides. Therefore, U.S. Patent 6,335,179 does not disclose the presently claimed invention in a manner sufficient to comply with the requirements fo the first paragraph of 35 U.S.C. 112 and the presently claimed invention does not have the

priority to the filing date of the corresponding U.S. Patent Application 09/185,373. The priority date for the presently claimed invention is February 4, 1999.

Information Disclosure Statement

7. The information disclosure statement filed October 14, 2005 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. The parent U.S. Patent Application 10/309,587 states that the references cited in the IDS can be found in U.S. Patent Application 09/756,459, however, the majority of the cited references were not found in U.S. Patent Application 09/756,459. Therefore, the references cited in the IDS not found in U.S. Patent Application 10/644,410; 10/309,587; or 09/756,459 have not been considered.

Specification

8. The disclosure is objected to because of the following informalities: In the first line of the Specification, it should be noted that U.S. Patent Application 10/309,587 is now U.S. Patent 6,764,835.

Appropriate correction is required.

Claim Interpretation

9. The presently claimed invention is directed to:

A method of providing a population of recombined nucleic acids comprising:

i. providing a population of oligonucleotides comprising at least one set of codon-varied oligonucleotides and wherein two or more members of the population comprise overlapping oligonucleotides,

ii. hybridizing at least two of the overlapping oligonucleotides to each other, and

iii. elongating members of the population of hybridized overlapping oligonucleotides.

The limitation that at least one member of the set of codon-varied oligonucleotides is chemically synthesized using at least trinucleotide sequences is considered to be a functional limitation only.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 2 and 34 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: For example, expressing the polypeptide encoded by the recombined nucleic acid and screening for a desired trait or property.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 2-4, 11, 23, 25-26, 34-36, and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Sondek et al. April 1992. A general strategy for random insertion and substitution mutagenesis: substoichiometric coupling of trinucleotide phosphoramidites. PNAS Vol. 89, pages 3581-3585.

Sondek et al. teach methods for inducing random, in-phase codon insertions across a defined segment of a cloned gene to provide a population of recombined nucleic acids (please

refer to the abstract). Sondek et al. teach providing a population of oligonucleotides comprising at least one set of codon-varied oligonucleotides (e.g. GCT, GGT, or trinucleotide phosphoramidites specifying varied alanine or a glycine codons which were custom-synthesized; please refer to the abstract and the Materials and Methods section), hybridizing at least two overlapping oligonucleotides (please refer to Figure 1 and page 3582), and elongating members (e.g. present claims 2-4 and 36; please refer to Figure 1 and page 3582). Sondek et al. also teaches providing mononucleotides, oligonucleotides, and trinucleotide phosphoramidite (e.g. present claim 11; please refer to Figure 1 and Materials and Methods). In addition, Sondek et al. teach in vitro synthesis of recombined nucleic acids (e.g. present claim 23; please refer to Materials and Methods). Furthermore, Sondek et al. teach that the population of oligonucleotides with sequence homology to wild-type sequences are utilized as primers for second-strand synthesis on a single-stranded DNA template in order to create recombined nucleic acids encoding mutagenized nuclease genes (e.g. PCR with a thermostable polymerase; present claims 25-26; please refer to page 3582, second column and page 3583, second column). Additionally, Sondek et al. teach that the mutagenized nuclease genes were selected for a deficiency in nuclease activity (e.g. present claim 34; please refer to page 3583, second column). Moreover, Sondek et al. teach staphylococcal nuclease gene with a consensus region (e.g. present claim 35; please refer to page 3583, second column). Sondek et al. also teach that the oligonucleotides are in equimolar amounts (e.g. present claim 39; please refer to the abstract). Therefore, one of ordinary skill in the art would have anticipated the presently claimed invention of claims 2-4, 11, 23, 25-26, 34-36, and 39 in view of the teachings of Sondek et al.

14. Claims 2-4, 11, 23, 25-26, 34-36, and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Ladner et al. U.S. Patent 5,223,409 issued June 29, 1993.

Ladner et al. teach methods for the construction, expression, and selection of mutated genes (please refer to column 7, lines 36-45). Ladner et al. teach methods making recombined nucleic acids utilizing populations of oligonucleotides comprising varied codons (e.g. present claim 2; please refer to column 8). In addition, Ladner et al. teach methods of providing recombined nucleic acids comprising providing variegated, chemically synthesized codon oligonucleotides (e.g. present claims 2 and 36; please refer to columns 41-50), hybridizing the variegated codon oligonucleotides to a template, and elongated via PCR or in vitro (e.g. present claims 2, 23, and 25-26; please refer to columns 50-53). Additionally, Ladner et al. teach selection of oligonucleotides with acceptable complementarity or homology and the coupling together of various oligonucleotides (e.g. present claims 3-4 and 11; please refer to column 37, lines 35-47 and columns 41-53). Furthermore, Ladner et al. teach screening for desired traits or properties including specific binding (e.g. present claim 34; please refer to columns 122-124). Ladner et al. also teach oligonucleotides encoding consensus regions of various miniproteins including antibodies, antibody fragments, and metal finger miniproteins (e.g. present claim 35; please refer to columns 25-30). Moreover, Ladner et al. teach that the oligonucleotides can be in equimolar amounts (e.g. present claim 39; please refer to column 38). Therefore, one of ordinary skill in the art would have anticipated the presently claimed invention of claims 2-4, 11, 23, 25-26, 34-36, and 39 in view of the teachings of Ladner et al.

15. Claims 2-4, 11, 23, 25-26, 34-36, and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Stemmer in Proceedings of the National Academy of Sciences, Volume 91, pages 10747-10751, published 1994.

Stemmer teaches a method of DNA shuffling by random fragmentation and reassembly (please refer to the abstract). Stemmer teaches providing DNA fragments from 10-50 base pairs at a denaturing temperature of 94°C (e.g. population of oligonucleotides of present claim 2), hybridizing at least three overlapping oligonucleotides in equimolar amounts containing consensus region(s) at 50-55°C, and elongating the hybridized overlapping oligonucleotides at 72°C (e.g. present claims 2, 35-36, and 39; please refer to pages 10747-10745, Introduction and "Materials and Methods" sections and Figures 1 and 5). In addition, Stemmer teaches selecting a first (e.g. murine IL-1β gene) and a second nucleic acid (e.g. human IL-1β gene) with some homology to be recombined (e.g. present claims 3-4; please refer to page 10748, IL-1β experiments section and Figure 1). In particular, Stemmer teaches that the provided nucleotides are oligonucleotides or mononucleotides (e.g. present claim 11; please refer to Figures 1 and 5). Furthermore, Stemmer teaches that the hybridizing step occurs in vitro and elongation is via a thermostable polymerase (e.g. present claims 23 and 25-26; please refer to page 10747). Moreover, Stemmer teaches DNA sequencing to select for recombined nucleic acids with a desired trait, mutation, or chimeras (e.g. present claim 34; please refer to pages 10748-10750). Overall, one of ordinary skill in the art would have anticipated the presently claimed invention of claims 2-4, 11, 23, 25-26, 34-36, and 39 in view of the teachings of Stemmer.

16. Claims 2-4, 11, 23, 25-26, 34-36, and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Stemmer U.S. Patent 5,605,793 filed February 17, 1994.

Stemmer teaches nucleic acid shuffling (please refer to "Abstract"). Stemmer teaches providing oligonucleotide fragments in a mixture (including equimolar amounts), hybridizing or annealing overlapping fragments, and elongating the hybridized fragments with a thermostable polymerase in vitro (e.g. present claims 2, 11, 23, 25-26, and 39; please refer to columns 3 and 7-8, Figures 1 and 5-7, and Examples 1-7). In addition, Stemmer teaches selecting at least a first and second nucleic acids with homology to be recombined (e.g. present claims 3-4; please refer to Examples 1-7). Furthermore, Stemmer teaches selecting for a desired trait or property (e.g. present claim 34; please refer to column 17, lines 53-67; columns 18, lines 57-67 and column 19, lines 1-16; and columns 25-26). Moreover, Stemmer teaches that the overlapping oligonucleotides comprise consensus regions and at least three oligonucleotides (please refer to Figures 6-7 and Example 7). Overall, one of ordinary skill in the art would have anticipated the presently claimed invention of claims 2-4, 11, 23, 25-26, 34-36, and 39 in view of the teachings of Stemmer.

Double Patenting

17. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

18. Claims 2-4, 11, 25-26, 34-35 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5, 10-11, 14-15, 18, and 20-21 of U.S. Patent No. 6,238,884 issued May 29, 2001 in view of Guatelli et al. April 1989 Clinical Microbiology Reviews 2(2): 217-226. Although the conflicting claims are not identical, they are not patentably distinct from each other because U.S. Patent No. 6,238,884 claims a method for producing a mutant polynucleotide (e.g. recombined nucleic acid of present claim 2) comprising providing codon-containing polynucleotides and degenerate oligonucleotides for each codon to be mutated and having homology with the codon-containing polynucleotides for amplification (e.g. providing, hybridizing, and elongating of present claim 2, present claim 3, homology of present claim 4, and coupling together oligonucleotides of present claim 11). Amplification is defined as increasing the number of copies of a polynucleotide (please refer to the specification column 7, lines 44-45) and PCR is utilized for amplification in Examples 3 and 5-6 in the specification. Guatelli et al. teach that PCR includes providing templates and primers (e.g. oligonucleotides), primer annealing (e.g. hybridization), and extension to amplify nucleic acids (please refer to Figure 1 and section "Methodology of sequence amplification by PCR" of Guatelli et al.). In addition, U.S. Patent 6,238,884 claims that the polynucleotide encoding a protein is expressed in a host cell via an expression vector (e.g. present claims 25-26 elongated

with a thermostable polymerase). U.S. Patent 6,238,884 also claims screening the recombined nucleic acids for a desired trait or property (e.g. present claim 34) and specific enzymatic activity (e.g. the recombined nucleic acid encodes an enzyme with a consensus region of present claim 35).

19. Claims 2-4, 11, 23, 25-26, 34, and 36 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 7-10 of U.S. Patent No. 6,171,820 issued January 9, 2001 in view of Guatelli et al. April 1989 Clinical Microbiology Reviews 2(2): 217-226. Although the conflicting claims are not identical, they are not patentably distinct from each other because while the present application is drawn to a method for providing recombined nucleic acids, U.S. Patent 6,171,820 is drawn to a method of producing mutant polypeptides comprising producing recombined nucleic acids. U.S. Patent 6,171,820 claims methods comprising subjecting codon-containing template polynucleotides to polymerase-based amplification in the presence of degenerate oligonucleotides with sequence homology and the degenerate structure NNN, NNG, or NNT (e.g. providing, hybridizing, and elongating of present claim 2, present claims 3-4, 11, 23, 25-26, and 36). Amplification is defined as increasing the number of copies of a polynucleotide (please refer to the specification column 7, lines 31-32) and PCR is utilized for amplification in Examples 3 and 5 in the specification. Guatelli et al. teach that PCR includes providing templates and primers (e.g. oligonucleotides), primer annealing (e.g. hybridization), and extension to amplify nucleic acids (please refer to Figure 1 and section "Methodology of sequence amplification by PCR" of Guatelli et al.). U.S. Patent 6,171,820 also claims screening for a desirable improvement (e.g. present claim 34).

20. Claims 2-4, 11, 23, 25-26, 34, and 36 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 3 and 6 of U.S. Patent No. 6,562,594 issued May 13, 2003 in view of Guatelli et al. April 1989 Clinical Microbiology Reviews 2(2): 217-226. Although the conflicting claims are not identical, they are not patentably distinct from each other because while the present application is drawn to a method for providing recombined nucleic acids, U.S. Patent 6,562,594 is drawn to methods of producing mutant polypeptides and hybrid polynucleotides comprising producing recombined nucleic acids. U.S. Patent 6,562,594 claims methods comprising subjecting codon-containing template polynucleotides to polymerase-based amplification in the presence of degenerate oligonucleotides with sequence homology and the degenerate structure NNN (e.g. providing, hybridizing, and elongating of present claim 2, present claims 3-4, 11, 23, 25-26, and 36). Amplification is defined as increasing the number of copies of a polynucleotide (please refer to the specification column 7, lines 12-13) and PCR is utilized for amplification in Examples 3 and 5 in the specification. Guatelli et al. teach that PCR includes providing templates and primers (e.g. oligonucleotides), primer annealing (e.g. hybridization), and extension to amplify nucleic acids (please refer to Figure 1 and section "Methodology of sequence amplification by PCR" of Guatelli et al.). U.S. Patent 6,562,594 also claims screening for a desirable improvement (e.g. present claim 34).

Future Correspondence

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amber D. Steele whose telephone number is 571-272-5538. The examiner can normally be reached Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ADS
January 24, 2006

ANDREW WANG
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

George C. Elliott, Ph.D
Director
Technology Center 1600